

**CLAIMS**

**I CLAIM:**

1. – 105. (cancelled)

106. (new) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

- a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and
- b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile; and
- c) selecting a perioperative course of action based on information from said genomic profile, wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure, thereby determining a risk for complications during said surgical procedure.

107. (new) The method of Claim 106, wherein said surgical procedure is the first surgical procedure for said subject.

108. (new) The method of Claim 106, wherein previous said surgical procedures on said patient have been with one or more complications.

109. (new) The method of Claim 106, wherein said course of action comprises administration of anesthesia during a surgical procedure.

110. (new) The method of Claim 109, wherein said anesthesia is general

anesthesia.

111. (new) The method of Claim 110, wherein said general anesthesia is inhalational anesthesia.

112. (new) The method of Claim 110, wherein said general anesthesia is intravenous anesthesia.

113. (new) The method of Claim 109, wherein said anesthesia is regional anesthesia.

114. (new) The method of Claim 113, wherein said regional anesthesia is spinal or epidural anesthesia.

115. (new) The method of Claim 106, wherein said surgical procedure is non-invasive surgery.

116. (new) The method of Claim 106, wherein said surgical procedure is invasive surgery.

117. (new) The method of Claim 106, wherein said course of action comprises administration of anesthesia during a medical procedure.

118. (new) The method of Claim 106, wherein said genomic profile comprises information pertaining to a pharmacodynamic risk.

119. (new) The method of Claim 106, wherein said genomic profile comprises information pertaining to a pharmacokinetic risk.

120. (new) The method of Claim 106, wherein said genomic profile comprises a presymptomatic diagnosis.

121. (new) The method of Claim 106, wherein said genomic profile comprises information pertaining to differential diagnosis of co-existing diseases.

122. (new) The method of Claim 106, wherein said two or more nucleic acid genetic markers comprise mutations in two or more genes, said genes selected from the group consisting of *BChE*, *CYP2D6*, *MTHFR*, *MTR*, *CBS*, *F2*, *F5*, *RYR1*, *CACNA1S*, and *CPT2*.

123. (new) The method of Claim 122, wherein said two or more nucleic acid genetic markers comprise 5 or more mutations in two or more genes.

124. (new) The method of Claim 122, where in said two or more nucleic acid genetic markers comprise 10 or more mutations in two or more genes.

125. (new) The method of Claim 106, wherein said genomic profile consists of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, TNF $\alpha$  and TNF $\beta$ .

126. (new) The method of Claim 106, further comprising the step of:  
d) using said genomic profile for selection of conditions for a surgical procedure carried out on said patient.

127. (new) A method for selecting conditions for a surgical procedure by screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

- a) providing a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;
- b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes known to be associated with two or more perioperative phenotypes to generate a genomic profile;

- c) selecting a surgical procedure treatment course of action based on information from said genomic profile; and
- d) subjecting said subject to a surgical procedure.

128. (new) The method of Claim 127, wherein said genetic markers are associated with a pharmacological response.

129. (new) The method of Claim 128, wherein said pharmacological response is to an anesthetic.

130. (new) The method of Claim 128, wherein said pharmacological response is to drugs used in anesthetic practice.

131. (new) The method of Claim 127, wherein said two or more nucleic acid genetic markers comprises a mutation in two or more genes associated with two or more conditions, said genes selected from the group consisting of *BChE*, *CYP2D6*, *MTHFR*, *MS*, *CBS*, *F2*, *F5*, *RYR1*, *CACNA1S*, and *CPT 2*.

132. (new) The method of claim 131, wherein said two or more nucleic acid genetic markers comprises 5 or more mutations in two or more genes.

133. (new) The method of claim 131, wherein said two or more nucleic acid genetic markers comprises 10 or more mutations in two or more genes.

134. (new) The method of Claim 127, wherein said genomic profile consists of alleles in genes encoding BChE, CYP2D6, MTHFR, MTR, CBS, F2, F5, RYR1, CACNA1S, and CPT2, TNF $\alpha$  and TNF $\beta$ .

135. (new) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure from known genetic variations comprising:

- a) obtaining a sample from a perioperative subject, said perioperative

subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and

- b) subjecting said sample to an assay for detecting genetic markers in genes clinically associated with conditions consisting of butyrylcholinesterase deficiency, impaired debrisoquine metabolism, sepsis, thrombosis, and malignant hyperthermia to generate a genomic profile;
- c) directing a physician to a perioperative treatment course of action based on information from said genomic profile for determining a risk for complications during a surgical procedure; and
- d) subjecting said subject to a surgical procedure.

136. (new) The method of Claim 135, wherein said physician is an anesthesiologist.

137. (new) The method of Claim 135, wherein said course of action comprises administration of anesthesia during a surgical procedure.

138. (new) The method of Claim 135, wherein said physician is a surgeon.

139. (new) The method of Claim 135, wherein said surgical procedure is non-invasive surgery.

140. (new) The method of Claim 135, wherein said surgical procedure is invasive surgery.

141. (new) The method of Claim 135, wherein the said two or more nucleic acid genetic markers comprises 5 or more mutations in two or more genes.

142. (new) The method of Claim 135, wherein the said two or more nucleic acid genetic markers comprises 10 or more mutations in two or more genes.

143. (new) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure from known genetic variations comprising:

- a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and
- b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes clinically associated with butyrylcholinesterase deficiency and impaired debrisoquine metabolism to generate a genomic profile;
- c) directing a physician to a perioperative treatment course of action based on information from said genomic profile for determining a risk for complications during a surgical procedure; and
- d) subjecting said subject to a surgical procedure.

144. (new) A method for selecting an appropriate anesthesia treatment during surgery, comprising:

- a) providing a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and
- a) subjecting said sample to an assay that detects a first marker in a first gene and a second marker in a second gene to generate assay results, wherein said markers are known to be associated with adverse responses to anesthesia treatment; and
- c) subjecting said subject to a surgical procedure, wherein said assay results are consulted by a physician in selecting an appropriate anesthesia treatment for said subject based on information from said assay results.

145. (new) The method of Claim 144, wherein said physician is an anesthesiologist.

146. (new) The method of Claim 144, wherein said selecting comprises selection of

dosages of anesthesia.

147. (new) The method of Claim 144, wherein said selecting comprises selection of anesthesia compounds.

148. (new) The method of Claim 144, wherein said selecting comprises selection of monitoring procedures.

149. (new) A method for providing a perioperative course of action to a clinician based on a patient's risk for complications during and after a surgical procedure associated with known genetic variations, comprising:

- a) obtaining consent from a patient to obtain and assay a sample from a perioperative subject for genetic variations, said patient being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure;
- b) obtaining said sample from said patient;
- c) forwarding said sample to a clinical laboratory;
- d) isolating DNA from said sample in said clinical laboratory;
- e) subjecting said DNA to an assay in said clinical laboratory for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure;
- f) forwarding the results of said genomic profile to said clinician;
- g) directing said clinician to a perioperative course of action for said patient based on said risk for complications during and after said surgical procedure based on information from said genomic profile;
- h) subjecting said patient to a surgical procedure based on said perioperative course action;
- i) distributing said results of said patient's said genomic profile according to said patient's preference; and
- j.) distributing said patient's said sample according to said patient's preference.

150. (new) The method of Claim 149, wherein said directing said clinician to said perioperative course of action comprises a computer program comprising instructions which direct a processor to analyze said results of said genomic profile.

151. (new) The method of Claim 150, wherein said instructions translate said results into information of predictive value for a clinician.

152. (new) The method of Claim 150, wherein said instructions translate said results into a risk assessment for treatment options.

153. (new) The method of Claim 150, wherein said instructions translate said result into recommendations for treatment options.

154. (new) The method of Claim 150, wherein said instructions generate a report for display to a clinician.

155. (new) The method of Claim 154, wherein said display is in the form of a report that can be printed.

156. (new) The method of Claim 154, wherein said display is in the form of a report on a computer monitor.

157. (new) The method of Claim 150, wherein said instructions are sufficient to receive, process and transmit said results of said genomic profile to and from said patient, a clinical laboratory and medical personnel.

158. (new) The method of Claim 157, wherein said transmission of said results uses an electronic communication system.

159. (new) The method of Claim 158, wherein said electronic communication system transmits said results to a distant computer system for processing.



160. (new) The method of Claim 150, wherein said instructions comprise information to optimize perioperative care that, based on at least the presence of variant alleles of two or more genes associated with two or more conditions selected from the group consisting of *BChE*, *CYP2D6*, *F5*, *F2*, *CACNAIS*, *MTHFR*, *MTR*, *MTRR*, *CBS*, *TNF $\alpha$*  and *TNF $\beta$* , directs said clinician to a specific perioperative clinical pathway for said patient.

161. (new) The method of Claim 149, wherein said perioperative course of action is an anesthesia treatment course of action.

162. (new) The method of Claim 161, wherein said anesthesia treatment course of action is a general anesthesia course of action.

163. (new) The method of Claim 162, wherein said general anesthesia treatment course of action is an inhalational anesthesia treatment course of action.

164. (new) The method of Claim 162, wherein said general anesthesia treatment course of action is an intravenous anesthesia treatment course of action.

165. (new) The method of Claim 162, wherein said general anesthesia treatment course of action is a combined inhalational and intravenous anesthesia treatment course of action.

166. (new) The method of Claim 161, wherein said anesthesia treatment course of action is a regional anesthesia treatment course of action.

167. (new) The method of Claim 161, wherein said anesthesia treatment course of action is a combined regional and general anesthesia treatment course of action.

168. (new) The method of Claim 149, wherein said perioperative treatment course of action is an anesthesia course of action during a medical procedure.

169. (new) The method of Claim 149, wherein said perioperative treatment course of action comprises selection of dosages of analgesic compounds.

170. (new) The method of Claim 169, wherein said selection comprises increasing the dosage of analgesic compounds metabolized by CYP2D6.

171. (new) The method of Claim 169, wherein said selection comprises decreasing the dosage of analgesic compounds metabolized by CYP2D6.

172. (new) The method of Claim 149, wherein said perioperative treatment course of action comprises prophylaxis for thrombosis.

173. (new) The method of Claim 172, wherein said prophylaxis comprises increasing prophylaxis for thrombosis associated with variant alleles of *F5*, *F2*, *MTHFR*, *MTR*, *MTRR*, and *CBS*.

174. (new) The method of Claim 172, wherein said prophylaxis comprises decreasing prophylaxis for thrombosis associated with variant alleles of *F5*, *F2*, *MTHFR*, *MTR*, *MTRR*, and *CBS*.

175. (new) The method of Claim 149, wherein said perioperative course of action comprises monitoring procedures.

176. (new) The method of Claim 149, wherein said perioperative treatment course of action comprises pre-operative phenotypic tests and consultations.

177. (new) The method of Claim 149, wherein said risk of complications provides a prognosis after an anesthesia treatment course of action.

178. (new) The method of Claim 149, wherein said perioperative course of action is a surgical treatment course of action.

179. (new) The method of Claim 178, wherein said surgical treatment course of action is a non-invasive surgical treatment course of action.

180. (new) The method of Claim 178, wherein said surgical treatment course of action is an invasive surgical treatment course of action.

181. (new) The method of Claim 149, wherein said risk of complications provides a prognosis after a surgical treatment course of action.

182. (new) The method of Claim 149, wherein said perioperative treatment course of action comprises a post-operative treatment course of action.

183. (new) The method of Claim 149, wherein said perioperative treatment course of action directs a clinician to a specific clinical pathway of medical intervention for said patient.

184. (new) The method of Claim 149, wherein said perioperative treatment course of action directs a clinician to a specific clinical pathway of anesthesia intervention for said patient.

185. (new) The method of Claim 149, wherein said assay comprises structure-specific cleavage of oligonucleotide probes assay.

186. (new) The method of Claim 149, wherein said assay comprises a kit for generating a perioperative genomic profile for a subject, comprising:

- a) reagents configured such that when exposed to a sample containing target nucleic acid from a perioperative subject, said subject being a patient scheduled for a surgical procedure that has not yet completed said

surgical procedure, are sufficient to detect the presence or absence of variant alleles in two or more genes associated with two or more conditions selected from the group consisting of *BChE*, *CYP2D6*, *F5*, *F2*, *CACNAIS*, *MTHFR*, *MTR*, *MTRR*, *CBS*, *TNF $\alpha$*  and *TNF $\beta$*  so as to generate a genomic profile for use in selecting a perioperative course of action for said subject; and

b) a computer program on a computer readable medium comprising instructions which direct a processor to analyze data derived from use of said reagents.

187. (new) The method of Claim 149, further comprising the step of encrypting said results of said genomic profile.

188. (new) The method of Claim 149, further comprising the step of decoding said results of said genomic profile.

189. (new) A method of screening a patient perioperatively to determine a risk for complications during a surgical procedure associated with known genetic variations comprising:

- a) obtaining a sample from a perioperative subject, said perioperative subject being a patient scheduled for a surgical procedure that has not yet completed said surgical procedure; and
- b) subjecting said sample to an assay for detecting two or more nucleic acid genetic markers in two or more genes associated with two or more conditions to generate a genomic profile, wherein said markers are selected by the criteria of analytical validity, clinical validity and clinical utility; and
- c) selecting a perioperative course of action based on information from said genomic profile, wherein said subjecting step occurs after said patient is scheduled for surgery but before completion of said surgical procedure, thereby determining a risk for complications during said surgical procedure;

- e) distributing said results of said patient's said genomic profile according to said patient's preference; and
- e) distributing said patient's said sample according to said patient's preference.

190. (new) The method of Claim 189, wherein said selecting of markers, said subjecting said sample to said assay, and said distributing of said results of said patient's said genomic profile is organized by an integrated electronic system.

191. (new) The method of Claim 189, further comprising the step of selecting said genetic markers from the group consisting of genetic markers of pharmacogenetic risk, genetic markers of co-existing symptomatic conditions, genetic markers of co-existing non-symptomatic conditions, genetic markers of outcomes of a surgical procedure, genetic markers of a patient in a specific group, genetic markers that predict postoperative outcomes, and genetic markers consisting of unique genomic identifiers.